Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S9	1267	thymosin	US-PGPUB; USPAT	OR	OFF	2004/12/15 08:09
S10	102	S9 near5 (gene$1 or sequence$1)	US-PGPUB; USPAT	OR	OFF	2004/12/15 08:09
S11	196	S9 adj beta	US-PGPUB; USPAT	OR	OFF	2004/12/15 08:10
S12	31	S10 and S11	US-PGPUB; USPAT	OR	OFF	2004/12/15 08:10

PGPUB-DOCUMENT-NUMBER: 20040213772

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040213772 A1

TITLE: Peptide factor

PUBLICATION-DATE: October 28, 2004

INVENTOR-INFORMATION:

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APPL-NO: 10/ 339271

DATE FILED: January 9, 2003

RELATED-US-APPL-DATA:

child 10339271 A1 20030109

parent continuation-of 09647117 20010123 US GRANTED

parent-patent 6602519 US

child 09647117 20010123 US

parent a-371-of-international PCT/GB99/00833 19990329 WO UNKNOWN

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
GB	9806632.7	1998GB-9806632.7	March 28, 1998
GB	0008903.7	2000GB-0008903.7	April 12, 2000

US-CL-CURRENT: 424/94.1

ABSTRACT:

The present invention relates to use of oxidised thymosin .beta.4 in therapy, more particularly in the treatment of diseases or conditions associated with an inflammatory response or septic shock. The present invention also provides pharmaceutical formulations comprising oxidised thymosin .beta.4 together with a suitable excipient.

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Summary of Invention Paragraph - BSTX (24):

[0024] Thymosin .beta.4 in an oxidised or non-oxidised form may be obtained from any suitable source, for example from steroid treated monocytes. Moreover, the thymosin .beta.4 may be derived from any suitable species, but is typically of mammalian origin, such as bovine, equine, murine or human origin. It is to be noted that bovine, equine, murine, rat and human thymosin .beta.4 are all identical in sequence. Thus, for example, bovine thymosin .beta.4 may

provide a suitable source of thymosin .beta.4 for subsequent oxidation and administration to other species, such as humans.

Summary of Invention Paragraph - BSTX (41):
[0041] According to the present invention there is also provided a synthetic oxidised thymosin .beta.4 comprising the peptide sequence of thymosin .beta.4 in oxidised form or physiologically active variant thereof.

Summary of Invention Paragraph - BSTX (48):
[0048] The invention further provides use of a nucleotide molecule having a sequence capable of encoding thymosin .beta.4 as described herein for subsequently preparing oxidised thymosin .beta.4.

Detail Description Paragraph - DETX (82):
[0167] Note: Cannot distinguish between Leu and Ile [LI] as they are isomers. Sequences corresponded exactly to tryptic fragments of human Thymosin Beta-4.

Claims Text - CLTX (19):
19. Synthetic oxidised peptide comprising a portion of the sequence of thymosin .beta.4, wherein at least the methionine is present and in oxidised form.

PGPUB-DOCUMENT-NUMBER: 20040158581

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040158581 A1

TITLE: Method for determination of co-occurences of attributes

PUBLICATION-DATE: August 12, 2004

INVENTOR-INFORMATION:

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APPL-NO: 10/ 478418

DATE FILED: November 21, 2003

PCT-DATA:
APPL-NO: PCT/CA02/00731
DATE-FILED: May 17, 2002
PUB-NO:
PUB-DATE:
371-DATE:
102(E)-DATE:

US-CL-CURRENT: 707/104.1

ABSTRACT:

A method, system, computer program selecting attribute sets of characterizing attributes of an object, selecting an attribute set of attributes of interest, assigning a likelihood for each characterized attribute set that the attribute set occurs when the attribute set of interest occurs (each likelihood determined using Bayesian computable classifiers on a dataset of attributes for actual samples), comparing each assigned likelihood against likelihood thresholds, and reporting the assigned likelihoods of the characterizing attribute set based on the likelihood thresholds. Markers may be identified for diagnosis and prognosis. Characterizing attributes may be gene expression levels and the attribute of interest may be drug sensitivity level, drug dose (absolute concentration or dose relative to some standard dose), dose of drug which causes half-maximal cellular growth rate, or logarithm base 10 (dose) where dose is the dose which yields half-maximal total cell mass accumulating.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority from U.S. patent application Ser. No. 60/291,928 filed May 21, 2001 by the same inventors under the same title, and from U.S. patent application Ser. No. 60/291,931 filed May 21, 2001 by the same inventors under the title Methods of Gene Analysis and Treating Cancer. U.S. patent application Ser. Nos. 60/291,928 and 60/291,931 are hereby incorporated herein by reference.

---------- KWIC ---------

Detail Description Paragraph - DETX (1118):
[0766] Gene: Human thymosin beta-4 mRNA complete cds Chr.20 [305890(IW) 5':W19923 3':N91268]

Detail Description Paragraph - DETX (2000):
[1254] Gene 2: Human thymosin beta-4 mRNA complete cds Chr.20 [305890 (IW) 5':W19923 3':N91268]

PGPUB-DOCUMENT-NUMBER: 20040101910

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040101910 A1

TITLE: Human Thymosin, beta15 gene, protein and uses thereof

PUBLICATION-DATE: May 27, 2004

INVENTOR-INFORMATION:

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APPL-NO: 10/ 726422

DATE FILED: December 3, 2003

RELATED-US-APPL-DATA:

child 10726422 A1 20031203

parent continuation-of 09874736 20010605 US ABANDONED

child 09874736 20010605 US

parent division-of 09369744 19990806 US GRANTED

parent-patent 6300479 US

child 09369744 19990806 US

parent division-of 09069484 19980429 US GRANTED

parent-patent 6017717 US

child 09069484 19980429 US

parent division-of 08931877 19970917 US GRANTED

parent-patent 5831033 US

child 08931877 19970917 US

parent division-of 08801796 19970214 US GRANTED

parent-patent 5721337 US

child 08801796 19970214 US

parent division-of 08664856 19960617 US GRANTED

parent-patent 5663071 US

US-CL-CURRENT: 435/7.1, 530/388.26

ABSTRACT:

The present inventors have now discovered that humans have a gene that encodes a novel protein of the thymosin .beta. family. This novel protein, herein referred to as thymosin .beta. 15, has the ability to bind and sequester G-actin, like other members of the thymosin .beta. family, but unlike what is known about other members it also directly regulates cell motility in prostatic carcinoma cells. The present invention is direct to an isolated cDNA encoding the human thymosin .beta. 15 gene (SEQ ID NO: 1) and have deduced the amino acid sequence (SEQ ID NO: 2).

---------- KWIC ---------

Abstract Paragraph - ABTX (1):

The present inventors have now discovered that humans have a gene that encodes a novel protein of the thymosin .beta. family. This novel protein, herein referred to as thymosin .beta. 15, has the ability to bind and sequester G-actin, like other members of the thymosin .beta. family, but unlike what is known about other members it also directly regulates cell motility in prostatic carcinoma cells. The present invention is direct to an isolated cDNA encoding the human thymosin .beta. 15 gene (SEQ ID NO: 1) and have deduced the amino acid sequence (SEQ ID NO: 2).

Title - TTL (1):

Human Thymosin, beta15 gene, protein and uses thereof

Summary of Invention Paragraph - BSTX (9):

[0007] We have now discovered that humans have a gene that encodes a novel protein of the thymosin .beta. family. This novel protein, herein referred to as thymosin .beta.15, has the ability to bind and sequester G-actin, like other members of the thymosin .beta. family, but unlike what is known about other members it also directly regulates cell motility in prostatic carcinoma cells. We have isolated a cDNA of the human thymosin, .beta.15 gene (SEQ ID NO: 1) and have deduced the amino acid sequence (SEQ ID NO: 2). We have shown that enhanced transcripts (mRNA) and expression of the thymosin .beta.15 gene in non-testicular cells has a high correlation to disease state in a number of cancers, such as prostate, lung, melanoma and breast cancer, particularly metastatic cancers. Accordingly, discovering enhanced levels of transcript or gene product in non-testicular tissues can be used in not only a diagnostic manner, but a prognostic manner for particular cancers.

Summary of Invention Paragraph - BSTX (10):

[0008] The present invention provides isolated nucleic acids (polynucleotides) which encode thymosin .beta.15 having the deduced amino acid sequence of SEQ ID. NO: 2 or a unique fragment thereof. The term "unique fragment" refers to a portion of the nucleotide sequence or polypeptide of the invention that will contain sequences (either nucleotides or amino acid residues) present in thymosin .beta.15 (SEQ ID NO: 2) but not in other member of the thymosin family. This can be determined when the hybridization profile of that fragment under stringent conditions is such that it does not hybridize to other members of the thymosin family. Such fragments can be ascertained from FIG. 3. A preferred set of unique fragments are those that contain, or contain polynucleotides that encode, amino acid 7 to 12 of SEQ ID NO: 2, amino acid 21 to 24 of SEQ ID NO: 2 and amino acid 36 to 45 of SEQ ID NO: 2. Preferably, the unique nucleotide sequence fragment is 10 to 60 nucleotides in length, more preferably, 20 to 50 nucleotides, most preferably, 30 to 50 nbtides. Preferably, the unique polypeptide sequence fragment is 4 to 20 amino acids in length, more preferably, 6 to 15 amino acids, most preferably, 6 to 1 0 amino acids.

Summary of Invention Paragraph - BSTX (15):
[0013] The present invention'further provides an isolated and purified human thymosin .beta.15 having the amino acid sequence of SEQ2 ID NO:

Summary of Invention Paragraph - BSTX (20):
[0018] The present invention further provides a method of treating a neoplastic cell expressing human thymosin .beta.15 by administering to the cell an effective amount of a compound which suppresses the activity or production of the human thymosin .beta.15 Preferably, the compound interferes with the expression of the human thymosin .beta.15 gene. Such compounds include, for example, antisense oligonucleotides, ribozymes, antibodies, including single chain antibodies and fragments thereof.

Brief Description of Drawings Paragraph - DRTX (2):
[0019] FIGS. 1A and 1B show differential mRNA display and Northern analysis of Dunning R-3327 rat prostatic adenocarcinoma variants. Total RNA from AT2.1 (lane 1), AT3.1 (lane 2) and AT6.1 (lane 3) cells were reverse- transcribed and amplified by PCR with a primer set, T.sub.11 AG and a 10 mer AGGGAACGAG (SEQ ID NO:3) in the presence of [.alpha.35-S]dATP. The PCR fragments were displayed on a 6% polyacrylamide gel and autoradiographed. The differentially expressed band is indicated by arrowhead. B. Northern blot analysis of thymosin .beta.15 gene. Two jig of poly (A) RNA was isolated from Dunning R-3327 variants AT2. I (lane 1), AT3.1 (lane 2), AT6.1 (lane 3), and Mat Lylu (lane 4), fractionated on a 1.1 % formaldehyde-agarose gel, transferred to Hybond-N +nylon membrane (Amersham) and hybridized with a random primed (Grillon C, et al., FEBS 1990, 274:30-34) .sup.32P-labeled T.beta.15 cDNA fragment. The same blot was hybridized with a rat.beta.-actin probe to demonstrate that equivalent amounts of RNA were loaded in each lane.

Brief Description of Drawings Paragraph - DRTX (13):
[0030] FIGS. 8A and 8B show Western analysis of thymosin, .beta.-GST fusion protein. FIG. 8A is a Coomasie staining of GST-T.beta. fusion proteins. FIG. 8B is a Western analysis of GST-T.mu. fusion proteins with affinity purified anti-T.beta.15 C-terminal peptide antibody. Lane 1:

Detail Description Paragraph - DETX (2):
[0035] A well characterized series of cell lines that show varying metastatic potential has been developed from the Dunning rat prostatic carcinoma (Isaacs, et al., Prostate 9, 261-281 and Bussebakers, et al., Cancer Res. 52,2916-2922 (1992)). Coffey and colleagues previously showed a direct correlation between cell motility and metastatic potential in the Dunning cell lines (Mohler, et al., Cancer Res. 48, 4312-4317 (1988), Parin, et al., Proc. Natl. Acad. Sci, USA 86, 1254-1258 (1989) and Mohler, et al., Cancer Metast. Rev 12, 53-67 (1993)). We compared gene expression in poorly metastatic and highly metastatic cell lines derived from Dunning rat prostate carcinoma using differential mRNA display. The results of these studies revealed the expression of a novel member of the thymosin beta family of 5 actin-binding molecules, thymosin .beta.15. Using this information, we isolated and sequenced a cDNA encoding human thymosin .beta.15.

Detail Description Paragraph - DETX (3):
[0036] Although members of the thymosin .beta. family have been shown to bind and sequester G-actin, they have not previously been demonstrated to alter cell motility. Our studies, however, reveal that this new member, thymosin .beta.15, directly regulates cell motility in prostatic carcinoma cells. We have shown that expression of thymosin .beta.15 is upregulated in highly

metastatic prostate cancer cell lines relative to poorly metastatic or nonmetastatic lines. In addition, thymosin .beta.15 was expressed in human prostate carcinoma specimens but not in normal human prostate. Although not wishing to be bound by theory, this indicates that .beta.15 plays a role in the process of metastatic transformation.

Detail Description Paragraph - DETX (4):
[0037] The present invention provides a polynucleotide sequence encoding all or part of thymosin .beta.15 having the deduced amino acid sequence of SEQ ID NO:2 or a unique fragment thereof. A-nucleotide sequence encoding human thymosin .beta.15 is set forth as SEQ ID NO:1.

Detail Description Paragraph - DETX (5):
[0038] The sequences of the invention may also be engineered to provide restriction sites, if desired. This can be done so as not to interfere with the peptide sequence of the encoded thymosin .beta.15, or may interfere to any extent desired or necessary, provided that the final product has the properties desired.

Detail Description Paragraph - DETX (26):
[0059] The antibody can be administered by a number of methods. One preferred method is set forth by Marasco and Haseltine in PCT W094/02610, which is incorporated herein by reference. This method discloses the intracellular delivery of a gene encoding the antibody, in this case the thymosin .beta.15 antibody. One would preferably use a gene 20 encoding a single chain thymosin .beta.15 antibody. The antibody would preferably contain a nuclear localization sequence, for example Pro-Lys-Lys-Lys-Arg-Lys-Val (SEQ ID NO:4) (Lawford, et al. Cell 46:575 (1986)]; Pro-Glu-Lys-Lys-Ile-Lys-Ser (SEQ ID NO:5) (Stanton, et al., Proc. Nat?. Acad. Sci. USA 83:1772 (1986)1, Gln-Pro-Lys-Lys-Pro (SEQ 25 ID NO:6) (Harlow, et al., Mol. Cell. Bio/. 5:1605 (1985)1; Arg-Lys-Lys-Arg (SEQ ID NO:7) for the nucleus. One preferably uses an SV40 nuclear localization signal. By this method one can intracellularly express a thymdsin .beta.15 antibody, which can block thymosin .beta.15 functioning in desired cells.

Detail Description Paragraph - DETX (29):
[0062] Affecting thymosin .beta.15 gene expression may also be achieved more directly, such as by blocking of a site, such as the promoter, on the genomic DNA.

Detail Description Paragraph - DETX (33):
[0066] In addition, ribozymes can be used to inhibit in vitro expression of thymosin .beta.15. For example, the nucleic acids of the invention can further be used to design ribozymes which are capable of cleaving a single-stranded nucleic acid encoding a .beta.15 protein, such as a thymosin .beta.15 mRNA transcript. A catalytic RNA (ribozyme) having ribonuclease activity can be designed which has specificity for an mRNA encoding thymosin .beta.15 based upon the sequence of a nucleic acid of the invention (e.g., SEQ ID NO: 1). For example, a derivative of a Tetrahymena L-19 IVS RNA can be constructed in which the base sequence of the active site is complementary to the base sequence to be cleaved in a thymosin .beta.15-encoding mRNA. See for example Cech, et al., U.S. Pat. No. 4,987,071; Cech, et al., U.S. Pat. No. 5,116,742. Alternatively, a nucleic acid of the invention could be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See for example Bartel, D. and Szostak, J. W. Science 261,1411-1418 (1993).

Detail Description Paragraph - DETX (59):
[0090] To obtain a full-length complementary DNA (cDNA) clone of this gene,

an AT3.1 cDNA library was screened using the originally cloned cDNA fragment from differential display as a probe. A positive clone with a 412 base pair insert was isolated, which contained a single open- reading frame encoding a 45 amino acid protein with a calculated molecular mass of 5304 (FIG. 2). The insert sizl-of the clone was approximately the same as the molecular size of the transcript seen in Northern analysis suggesting that the clone contained the full length gene sequence. A computer assisted homology search against the Genebank and EMBL DNA databases revealed that the novel gene shared 49% nucleotide sequence homology with rat thymosins ,4 and 610. Alignment of the deduced amino acid sequence of the cloned gene with members of the thymosin , family (Mihelic, M. & Voelter, Amino Acids 6, 1-13 (1994) showed 68% homology with thymosin .beta.4, 62% with thymosin P10 and 60% with .beta.9, .beta.11 and .beta.12 (FIG. 3). The results suggest that we have cloned a novel .beta.thymosin, now named thymosin .beta.15, from rat prostatic carcinoma cells.

Detail Description Paragraph - DETX (60):

[0091] Hydropathy analysis of the thymosin .beta.15 protein sequence revealed no apparent membrane-spanning or membrane-associated regions and no amino-terminal signal sequence. The protein is highly hydrophilic with an estimated isoelectric point of 5.14 and contains regions common to all members of the thymosin .beta. family. All .beta.-thymosin family members previously studied, for example, have a putative actin binding region (LKKTET) 16 residues from the amino terminus (Vancompernolle, et al., EMBO J. 11, 4739-4746 (1992), Troys, et al., EMBO J. 15, 201-210 (1 996). Thymosin 15 also has such a region, although the glutamic acid residue is replaced by an asparagine residue to form LKKTNT (FIG. 3). The principal region of nonconformity between members of the thymosin 6 family occurs at the carboxyl terminus and the thymosin .beta.15 sequence as well shows no significant homology in this region with other family members.

Detail Description Paragraph - DETX (61):

[0092] Members of the 6-thymosin family may be independently expressed in different tissues (Un, et al., J. Biol. Chem. 266, 23347-23353 (1991), Voisin, et al. J. Neurochem. 64, 109-120 (1995). Although thymosin,.beta.15 is differentially expressed in the prostate carcinoma cell lines tested, all of these lines expressed equivalent levels of thymosins f4 and 81 0 by RT-PCR analysis (FIG. 1 1). The tissue distribution of thymosin .beta.15 mRNA was examined in the major organs of the rat. No expression of thymosin .beta.15 was detected in the heart, brain, lung, spleen, liver, skeletal muscle and kidney, whereas high expression was found in the testis (FIG. 4). Southern (DNA) analysis of Hind IIII-, EcoR I- and Pst I-restricted DNA from AT2.1 and AT3.1 cells with thymosin .beta.15 cDNA probe revealed no gross structura; alteration of the thymosin .beta.15 gene in the tumor cells (data not shown). These results demonstrate that a novel member of the thymosin 8 family is upregulated in metastatic rat prostatic carcinoma cell lines, whereas expression of other thymosin .beta. family members (.beta.4 and .beta.10) remains unchanged.

Detail Description Paragraph - DETX (63):

[0094] DNase I digested 5 .beta.mg of total RNA from human prostatic carcinoma cell line PC-3 was,reverse transcribed using cDNA Cycling Kit (Invitrogen). The reverse transcription mixture was purified with a Spin Column 300 (Pharmocia, Piscataway, NY). 10 .beta.l of purified cDNA reaction was amplified with primers FI (5'-TATCAGCTAGTGGCTGCACCCGCG-3') (SEQ ID NO:8) and RI (5'-AAATGCT GACCTTrCAGTCAGGGT-3') (SEQ ID NO:9) designed to anneal to the outer ends of the thymosin .beta.15 sequence. PCR amplification was performed in 50 .beta.of PCR reaction buffer (50 mM KCI, 10 mM Tris (pH 8.5], 1.5 mM MgCI2) with 1 mM of dNTPs, 50 pmol of each primer, and 2.5 U of Taq

polymerase (GltCO BRL), overlaid with 50 pl of mineral oil (Sigma). The PCR profile was 94.degree. C., 30 sec; 60.degree. C., 30 sec; and 72.degree. C., 2 min for 30 cycles. Control studies of the RT-PCR were conducted using aliquats from the same samples and amplified with primers to the,B-actin gene (Clontech, Palo Alto, CA). Amplification products were separated on 1.6% agarose gels. The amplified PCR product was ligated to pCR using TA cloning kit (Invitrogen, San Diego, (CA), and then DNA sequenced. The sequence of the PCR product of human prostatic carcinoma cells amplified by the thymosin .beta.15 primers was surprisingly 100% identical to the thymosin .beta.15 sequence obtained from the rat prostatic carcinoma cells. Expression of T.beta.15 mRNA in human prostat cancer

Detail Description Paragraph - DETX (64):

[0095] To determine whether this thymosin family member may be expressed in human prostate cancer, we examined human prostatic carcinoma cell line PC-3 by RT-PCR with forward and reverse primers for thymosin .beta.15 The PC-3 cells showed a low level of thymosin .beta.15 expression. The DNA sequence of the amplified PCR product was 100% identical to the rat thymosin .beta.15 sequence. We conducted in situ hybridization study on samples from patients with varying grades of prostatic carcinomas using a thymosin .beta.15 probe. The tissue sections allowed direct comparison of normal and malignant elements on the same samples. The stromal elements within and around the tumor cell masses, as well as the nonmalignant prostatic epithelium adjacent to the tumor showed little background hybridization with the thymosin .beta.15 antisense probe. In contrast, specific tumor cell islands exhibited a strong specific thymosin .beta.15 signal when probed with antisense (FIG. 5A, small arrow) but not with a sense RNA probe (data not shown). Although nearly all of the tumor cells in the positive islands expressed thymosin .beta.15 mRNA, not all patient specimens were positive and not all islands in a single prostate were positive (FIG. 5A, large arrow). The majority of the negative tumor cells were in 20 non-invasive in situ carcinomas whereas highly invasive tumors were consistently positive (FIG. 58). Thus a novel P thymosin, first detected in metastatic rat prostate carcinoma cell lines, is upregulated in human prostate cancer.

Detail Description Paragraph - DETX (68):

[0099] To determine whether thymosin .beta.15 expression had an effect on cell motility, we transfected highly motile AT3.1 cells with a eukaryotic expression vector (pcDNA3) containing the thymosin .beta.15 gene in antisense orientation driven by the constitutive human cytomegalovirus promoter. The transfected cells growing in selective (G418) media were examined for expression of antisense transcripts of the thymosin .beta.15 gene by strand-specific polymerase chain reaction (PCR) amplification (Zhou, et al., CancerRes. 52, 4280-4285 (1992). Analysis of cell motility in a multiwell Boyden chamber apparatus (Boyden, S. V., J. Exp. Med. 115, 453-466 (1962)) using fetal bovine serum as a migration stimulus revealed that the motility of the transfectants which showed expression of antisense transcripts was significantly reduced relative to the vector-only controls (FIG. 7A). Two antisense transfected clones which did not express antisense transcripts failed to show any decreased rate of cell motility (data not shown). In a further experiment, poorly motile AT2.1 cells, transfected with sense thymosin .15 constructs and confirmed to express thymosin .beta.15 by Northern analysis, were shown to have significantly increased stimulated motility relative to their vector controls (FIG. 7B). Both the sense and antisense thymosin .beta.15 transfectants showed similar rates of cell proliferation relative to controls suggesting differential specificity for different cellular events (FIG. 7C). The results demonstrate that thymosin 815, which is upregulated in the highly motile AT3.1 and AT6.1 Dunning tumor cell lines, is a positive regulator of cell motility which is an important component of cancer

metastasis.

Claims Text - CLTX (7):
6. An isolated and purified human thymosin .beta.15 having the amino acid sequence set forth in SEQ ID NO.: 2.

Claims Text - CLTX (9):
8. An isolated polynucleotide encoding human thymosin .beta.15 comprising the amino acid sequence as set forth in SEQ ID NO:2.

Claims Text - CLTX (15):
14. An isolated polynucleotide encoding human thymosin ..beta.15 having the nucleotide sequence of nucleotides 98-232 of SEQ ID NO: 1, or the complement thereto.

Claims Text - CLTX (19):
18. The method of claim 17, wherein the compound interferes with the expression of the human thymosin .beta.15 gene.

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PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040072160 A1

TITLE: Molecular toxicology modeling

PUBLICATION-DATE: April 15, 2004

INVENTOR-INFORMATION:

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APPL-NO: 10/ 152319

DATE FILED: May 22, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60292335 20010522 US

non-provisional-of-provisional 60297523 20010613 US

non-provisional-of-provisional 60298925 20010619 US

non-provisional-of-provisional 60303810 20010710 US

non-provisional-of-provisional 60303807 20010710 US

non-provisional-of-provisional 60303808 20010710 US

non-provisional-of-provisional 60315047 20010828 US

non-provisional-of-provisional 60324928 20010927 US

non-provisional-of-provisional 60330867 20011101 US

non-provisional-of-provisional 60330462 20011022 US

non-provisional-of-provisional 60331805 20011121 US

non-provisional-of-provisional 60336144 20011206 US

non-provisional-of-provisional 60340873 20011219 US

non-provisional-of-provisional 60357843 20020221 US

non-provisional-of-provisional 60357842 20020221 US

non-provisional-of-provisional 60357844 20020221 US

non-provisional-of-provisional 60364134 20020315 US

non-provisional-of-provisional 60370206 20020408 US

non-provisional-of-provisional 60370247 20020408 US

non-provisional-of-provisional 60370144 20020408 US

non-provisional-of-provisional 60371679 20020412 US

non-provisional-of-provisional 60372794 20020417 US

US-CL-CURRENT: 435/6, 435/91.2 , 436/84

ABSTRACT:

The present invention is based on the elucidation of the global changes in gene expression and the identification of toxicity markers in tissues or cells exposed to a known renal toxin. The genes may be used as toxicity markers in drug screening and toxicity assays. The invention includes a database of genes characterized by toxin-induced differential expression that is designed for use with microarrays and other solid-phase probes.

RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Applications 60/292,335; 60/297,523; 60/298,925; 60/303,810; 60/303,807; 60/303,808; 60/315,047; 60/324,928; 60/330,867; 60/330,462; 60/331,805; 60/336,144; 60/340,873; 60/357,843; 60/357,842; 60/357,844; 60/364,134; 60/370,206; 60/370,247; 60/370,144; 60/371,679; and 60/372,794, all of which are herein incorporated by reference in their entirety. This application is also related to U.S. application Ser. Nos. 09/917,800 and 10/060,087, both of which are also herein incorporated by reference in their entirety.

---------- KWIC ---------

Detail Description Table CWU - DETL (31):

3,4- hydroxyanthranilate 3,4- dioxygenase dioxygenase (Haao), mRNA. Length = 1254 1744 16375 NM_020976 g Rattus norvegicus kidney- kidney-specific membrane protein specific membrane protein (NX-17), mRNA. Length = 1181 1745 20816 NM_021261 k, General Rattus norvegicus thymosin, thymosin beta-10 beta 10 (Tmsb10), mRNA. Length = 539 1746 15335 NM_021264 a Rattus norvegicus ribosomal ribosomal protein L35a protein L35a (Rpl35), mRNA. Length = 348 1747 18729 NM_021578 k, z Rattus norvegicus transforming growth factor beta-1 transforming growth factor gene beta-1 gene (Tgfb1), mRNA Length = 1585 1748 19060 NM_021587 cc Rattus norvegicus transforming growth factor-beta (TGF- transforming growth factor- beta) masking protein large subunit beta (TGF-beta) masking protein large subunit (Ltbp1), mRNA. Length = 6244 1749 17324 NM_021593 o, General Rattus norvegicus kynurenine 3-hydroxylase kynurenine 3-hydroxylase (Kmo), mRNA. Length = 1733 1750 19679 NM_021653 General Rattus norvegicus Thyroxine Thyroxine deiodinase, type I deiodinase, type I (Dio1), mRNA. Length = 2106 1750 19678 NM_021653 a, v Rattus norvegicus Thyroxine Thyroxine deiodinase, type I General deiodinase, type I (Dio1), mRNA Length = 2106 1751 19665 NM_021688 u, General Rattus norvegicus putative putative potassium channel TWIK potassium channel TWIK (Kcnk1), mRNA. Length = 1582 1752 19667 NM_021690 m Rattus norvegicus cAMP- cAMP-regulated guanine nucleotide regulated guanine nucleotide exchange factor I (cAMP-GEFI) exchange factor I (cAMP- GEFI) (Epac), mRNA. Length = 3373 1754 22916 NM_021740 a Rattus norvegicus prothymosin alpha prothymosin

alpha(Ptma), mRNA Length = 1182 1755 19710 NM_021744 t Rattus norvegicus CD14 CD14 antigen antigen (Cd14), mRNA. Length = 1591 1755 19711 NM_021744 t Rattus norvegicus CD14 CD14antigen antigen (Cd14), mRNA Length = 1591 1756 19712 NM_021745 r Rattus norvegicus farnesoid farnesoid X activated receptor X activated receptor (LOC60351), mRNA. Length = 2070 1757 1962 NM_021750 j, k, y, z Rattus norvegicus cysteine- Rattus norvegicus cca2 mRNA, sulfinate decarboxylase complete cds (Csad), mRNA Length = 2413 1757 19824 NM_021750 a, bb Rattus norvegicus cysteine- cysteine-sulfinate decarboxylase sulfinate decarboxylase (Csad), mRNA. Length = 2413 1758 25198 NM_021754 h Rattus norvegicus Nopp 140 Nopp140 associated protein associated protein (Nap65), mRNA. Length = 1980 1758 20035 NM_021754 b, n, s, v, Rattus norvegicus Nopp 140 Nopp140 associated protein General associated protein (Nap65), mRNA Length = 1980 1759 20090 NM_021757 m Rattus norvegicus pleiotropic pleiotropic regulator 1 regulator 1 (Plrg1), mRNA. Length = 1545 1760 17885 NM_021765 aa Rattus norvegicus beta beta prime COP prime COP (Copb), mRNA. Length = 3025 1762 20161 NM_021836 cc, Rattus norvegicus jun B jun B proto-oncogene General proto-oncogene (Junb), mRNA. Length = 1035 1764 1203 NM_021997 k, z Rattus norvegicus cytoplasmic linker 2 cytoplasmic linker 2 (Cyln2), mRNA Length = 4847 1765 23151 NM_022005 b Rattus norvegicus FXYD FXYD domain-containing ion transport domain-containing ion regulator 6 transport regulator 6 (Fxyd6), mRNA. Length = 1711 1767 17101 NM_022179 bb Rattus norvegicus Hexokinase 3 Hexokinase 3 (Hk3), mRNA Length = 3692 1767 17100 NM_022179 bb Rattus norvegicus Hexokinase 3 Hexokinase 3 (Hk3), mRNA. Length = 3692 1768 20257 NM_022180 w, Rattus norvegicus Hepatic Hepatic nuclear factor 4 (alpha General nuclear factor 4(alpha transcription factor 4) (Hnf4a), mRNA. Length = 1446 1768 25699 NM_022180 i Rattus norvegicus Hepatic Hepatic nuclear factor 4 (alpha nuclear factor 4(alpha transcription factor 4) transcription factor 4) (Hnf4a), mRNA. Length = 1446 1768 10860 NM_022180 p Rattus norvegicus Hepatic ESTs nuclear factor 4(alpha transcription factor 4) (Hnf4a), mRNA. Length = 1446 1769 23780 NM_022183 k, x Rattus norvegicus topoisomerase (DNA) II alpha topoisomerase (DNA) II alpha (Top2a), mRNA Length = 6052 1770 20312 NM_022224 o Rattus norvegicus resiniferatoxin-binding, resiniferatoxin-binding, phosphotriesterase-related protein phosphotriesterase-related protein (Rpr1), mRNA Length = 1050 1771 6585 NM_022266 d, p, cc Rattus norvegicus connective tissue growth factor connective tissue growth factor (Ctgf), mRNA Length = 2345 1772 17161 NM_022298 i, v, cc, Rattus norvegicus alpha- alpha-tubulin General tubulin (Tuba 1), mRNA. Length = 1617 1772 17162 NM_022298 u Rattus norvegicus alpha- alpha-tubulin tubulin (Tuba1), mRNA. Length = 1617 1772 17160 NM_022298 u Rattus norvegicus alpha- alpha-tubulin tubulin (Tuba1), mRNA. Length = 1617 1772 17158 NM_022298 q Rattus norvegicus alpha- alpha-tubulin tubulin (Tuba 1), mRNA. Length = 1617 1773 11454 NM_022381 i, aa, Rattus norvegicus Proliferating cell nuclear antigen General Proliferating cell nuclear antigen (Pcna), mRNA. Length = 1160 1773 11455 NM_022381 l, General Rattus norvegicus Proliferating cell nuclear antigen Proliferating cell nuclear antigen (Pcna), mRNA. Length = 1160 1774 13480 NM_022390 s Rattus norvegicus quinoid quinoid dihydropteridine reductase dihydropteridine reductase (Qdpr), mRNA Length = 1307 1775 15184 NM_022391 z Rattus norvegicus pituitary pituitary tumor transforming gene tumor-transforming 1 (Pttg1), mRNA Length = 974 1776 22413 NM_022392 h Rattus norvegicus growth growth response protein (CL-6) response protein (CL-6) (LOC64194), mRNA. Length = 2410 1776 22414 NM_022392 n Rattus norvegicus growth growth response protein (CL-6) response protein (CL-6) (LOC64194), mRNA. Length = 2410 1777 22499 NM_022393 t Rattus norvegicus Gal/GalNAc-specific lectin macrophage galactose N- acetyl-galactosamine specific lectin (Mgl), mRNA. Length = 1358 1779 24537 NM_022399 e Rattus norvegicus calreticulin calreticulin (Calr), mRNA. Length = 1882 1779 24539 NM_022399 y Rattus norvegicus calreticulin calreticulin (Calr), mRNA. Length = 1882 1780 1141 NM_022401 o, General Rattus norvegicus plectin plectin (Plec1), mRNA Length = 15,231

1781 1069 NM_022402 g Rattus norvegicus acidic acidic ribosomal protein P0 ribosomal protein P0 (Arbp), mRNA Length = 1046 1782 8211 NM_022500 j, n, s Rattus norvegicus ferritin ferritin light chain 1 light chain 1 (Ftl1), mRNA. Length = 552 1782 8212 NM_022500 n, s Rattus norvegicus ferritin ferritin light chain 1 light chain 1 (Ftl1), mRNA. Length = 552 1783 6815 NM_022503 s Rattus norvegicus cytochrome c oxidase subunit VIIa 3 cytochrome c oxidase subunit VIIa 3 (Cox7a3), mRNA. Length = 460 1784 4259 NM_022504 q, w Rattus norvegicus ribosomal ribosomal protein L36 protein L36 (Rpl36), mRNA. Length = 364 1785 1611 NM_022509 j Rattus norvegicus survival survival motor neuron motor neuron (Smn), mRNA. Length = 1243 1786 2236 NM_022512 y, z Rattus norvegicus short short chain acyl-coenzyme A chain acyl-coenzyme A dehydrogenase dehydrogenase (Acads), mRNA Length = 1749 1787 3026 NM_022514 a Rattus norvegicus ribosomal ribosomal protein L27

Detail Description Table CWU - DETL (35):

ribosomal protein S9 (Rps9), mRNA Length = 688 1879 10878 NM_031110 q, bb Rattus norvegicus ribosomal ribosomal protein S11 protein S11 (Rps11), mRNA. Length = 534 1880 19162 NM_031111 aa Rattus norvegicus ribosomal ribosomal protein S21 protein S21 (Rps21), mRNA. Length = 359 1880 19161 NM_031111 a, bb Rattus norvegicus ribosomal ribosomal protein S21 protein S21 (Rps21), mRNA Length = 359 1881 24615 NM_031112 a, y Rattus norvegicus ribosomal ribosomal protein S24 protein S24 (Rps24), mRNA. Length = 466 1882 20839 NM_031113 a, q Rattus norvegicus ribosomal ribosomal protein S27a protein S27a (Rps27a), mRNA Length = 552 1883 19040 NM_031114 l, m, Rattus norveglcus S-100 S-100 related protein, clone 42C General related protein, clone 42C (S100A10), mRNA Length = 573 1884 16349 NM_031115 u Rattus norvegicus secretin secretin receptor receptor (Sctr), mRNA. Length = 1796 1885 14970 NM_031127 General Rattus norvegicus sulfite sulfite oxidase oxidase (Suox), mRNA. Length = 1777 1886 1814 NM_031134 n, q Rattus norvegicus thyroid thyroid hormone receptor hormone receptor alpha (Thra1), mRNA. Length = 2460 1887 13359 NM_031135 General Rattus norvegicus TGFB TGFB inducible early growth response inducible early growth response (Tieg), mRNA. Length = 3115 1888 15052 NM_031136 a Rattus norvegicus thymosin thymosin beta-4 beta-4 (Tmsb4x), mRNA. Length = 686 1888 19359 NM_031136 a Rattus norvegicus thymosin EST beta-4 (Tmsb4x), mRNA Length = 686 1889 15185 NM_031140 General Rattus norvegicus vimentin vimentin (Vim), mRNA. Length = 1796 1890 21625 NM_031144 a, e Rattus norvegicus cytoplasmic beta-actin cytoplasmic beta-actin (Actx), mRNA. Length = 1128 1891 238 NM_031152 bb Rattus norvegicus RAB11a, RAB11a, member RAS oncogene member RAS oncogene family family (Rab11a), mRNA. Length = 895 1891 240 NM_031152 bb Rattus norvegicus RAB11a, RAB11a, member RAS oncogene member RAS oncogene family family (Rab11a), mRNA. Length = 895 1892 15277 NM_031237 g Rattus norvegicus ubiquitin- ubiquitin-conjugating enzyme E2D 3 conjugating enzyme E2D 3 (homologous to yeast UBC4/5) (homologous to yeast UBC4/5) (Ube2d3), mRNA Length = 1531 1893 18083 NM_031315 q Rattus norvegicus acyl-CoA R. norvegicus mRNA for mitochondrial thioesterase 1, cytosolic very-long-chain acyl-CoA thioesterase (Cte1), mRNA Length = 1591 1893 1858 NM_031315 q Rattus norvegicus acyl-CoA R. norvegicus mRNA for mitochondrial thioesterase 1, cytosolic very-long-chain acyl-CoA (Cte1), mRNA Length = 1591 thioesterase, acyl-CoA thioesterase 1, cytosolic 1894 15663 NM_031318 General Rattus norvegicus t-complex t-complex testis expressed 1 testis expressed 1 (Tctex1), mRNA. Length = 698 1895 1422 NM_031324 bb, Rattus norvegicus prolyl prolyl endopeptidase General endopeptidase (Prep), mRNA Length = 2743 1896 18597 NM_031325 g, bb Rattus norvegicus UDP- UDP-glucose dehydrogeanse glucose dehydrogeanse (Ugdh), mRNA Length = 2318 1897 11259 NM_031327 i, cc Rattus norvegicus cysteine cysteine rich protein 61 General rich protein 61 (Cyr61), mRNA. Length = 1871 1898 4235 NM_031330 General Rattus norvegicus heterogeneous nuclear heterogeneous nuclear ribonucleoprotein A/B ribonucleoprotein A/B (Hnrpab), mRNA Length = 3061

1899 18375 NM_031331 l, m Rattus norvegicus proteasome (prosome, macropain) proteasome (prosome, 26S subunit, non-ATPase, 4 macropain) 26S subunit, non-ATPase, 4 (Psmd4), mRNA. Length = 1334 1900 3519 NM_031334 cc Rattus norvegicus E- E-cadherin cadherin (Cdh1), mRNA Length = 4396 1901 20698 NM_031357 b Rattus norvegicus ceroid- lipofuscinosis, neuronal 2 (Cln2), mRNA. Length = 2485 1903 634 NM_031509 n Rattus norvegicus Glutathione-S-transferase, alpha type Glutathione-S-transferase, (Ya) alpha type (Ya) (Gsta1), mRNA. Length = 1178 1903 25525 NM_031509 n Rattus norvegicus Glutathione-S-transferase, alpha type Glutathione-S-transferas-e, (Ya) alpha type (Ya) (Gsta1), mRNA. Length = 1178 1903 25069 NM_031509 b, n, w Rattus norvegicus Glutathione-S-transferase, alpha type (Ya) (Gsta1), mRNA. Length = 1178 1903 635 NM_031509 z Rattus norvegicus Glutathione-S-transferase, alpha type Glutathione-S-transferas- e, (Ya) alpha type (Ya) (Gsta1), mRNA. Length = 1178 1904 848 NM_031517 t Rattus norvegicus Met proto- Met proto-oncogene oncogene (Met), mRNA. Length = 4189 1905 1872 NM_031523 a Rattus norvegicus Nerve Nerve growth factor, gamma growth factor, gamma polypeptide polypeptide (Ngfg), mRNA. Length = 873 1905 16245 NM_031523 a, d, u, Rattus norvegicus Nerve Rattus norvegicus (clone RSKG50) growth factor, gamma kallikrein mRNA, 3' end polypeptide (Ngfg), mRNA. Length = 873 1905 16244 NM_031523 a Rattus norvegicus Nerve Rattus norvegicus (clone RSKG50) growth factor, gamma kallikrein mRNA, 3' end polypeptide (Ngfg), mRNA. Length = 873 1906 9370 NM_031527 w Rattus norvegicus Protein Protein phosphatase type 1 alpha, phosphatase type 1 alpha, catalytic subunit catalytic subunit (Ppp1ca), mRNA Length = 1392 1907 20448 NM_031530 General Rattus norvegicus Small Small inducible gene JE inducible gene JE (Scya2), mRNA. Length = 780 1907 20449 NM_031530 General Rattus norvegicus Small Small inducible gene JE inducible gene JE (Scya2), mRNA Length = 780 1908 14633 NM_031533 u Rattus norvegicus Androsterone UDP-Androsterone UDP- glucuronosyltransferase glucuronosyltransferase (Ugt2b2), mRNA. Length = 1593 1909 16048 NM_031541 f Rattus norvegicus CD36 CD36 antigen (collagen type I antigen (collagen type I receptor, thrombospondin receptor)-receptor, thrombospondin like 1 (scavanger receptor class B receptor)-like 1 (scavanger type 1) receptor class B type 1) (Cd36l1), mRNA. Length = 2497 1910 4011 NM_031543 c, q Rattus norvegicus Cytochrome P450, subfamily 2e1 Cytochrome P450, subfamily (ethanol-inducible) 2e1 (ethanol-inducible) (Cyp2e1), mRNA. Length = 1624 1910 4010 NM_031543 c, q Rattus norvegicus Cytochrome P450, subfamily 2e1 Cytochrome P450, subfamily (ethanol-inducible) 2e1 (ethanol-inducible) (Cyp2el), mRNA. Length = 1624 1910 4012 NM_031543 q Rattus norvegicus Cytochrome P450, subfamily 2e1 Cytochrome P450, subfamily (ethanol-inducible) 2e1 (ethanol-inducible) (Cyp2e1), mRNA. Length = 1624 1911 28 NM_031546 General Rattus norvegicus Regucalcin Regucalcin (Rgn), mRNA Length = 1605 1912 24640 NM_031548 h, cc Rattus norvegicus Sodium Sodium channel, nonvoltage-gated 1, channel, nonvoltage-gated 1, alpha (epithelial) alpha (epithelial) (Scnn1a), mRNA. Length = 3081 1913 17149 NM_031549 x Rattus norvegicus Transgelin Transgelin (Smooth muscle 22 (Smooth muscle 22 protein) protein) (Tagln), mRNA. Length = 1186 1913 17151 NM_031549 x Rattus norvegicus Transgelin Transgelin (Smooth muscle 22 (Smooth muscle 22 protein) protein) (Tagln), mRNA Length = 1186 1914 13105 NM_031552 w Rattus norvegicus Adducin Adducin 3, gamma 3, gamma (Add3), mRNA. Length = 2246 1915 15411 NM_031559 d, r Rattus norvegicus Carnitine Carnitine palmitoyltransferase 1 alpha, palmitoyltransferase 1 alpha, liver isoform liver isoform (Cpt1a), mRNA Length = 4377 1916 16164 NM_031563 a, y Rattus norvegicus Y box Y box protein 1 protein 1 (Ybx1), mRNA.

Detail Description Table CWU - DETL (112):

transporters), member 3, solute carrier family 12, member 1, solute carrier family 12, member 3 1730 1301 NM_019349 c 1731 3776 NM_019354 a, u ESTs, Moderately similar to BMCP_HUMAN BRAIN MITOCHONDRIAL CARRIER PROTEIN-1 [H. sapiens], RIKEN cDNA 3632410G24 gene, RIKEN cDNA 4933433D23

gene, expressed sequence AW108044, solute carrier family 25 (mitochondrial carrier, brain), member 14, solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 10, solute carrier family 25 (mitochondrial carrier, ornithine transporter), member 15, uncoupling protein 2 (mitochondrial, proton carrier), uncoupling protein 2, mitochondrial 1732 4592 NM_019356 General RIKEN cDNA 0910001O23 gene, eukaryotic translation initiation factor 2, subunit 1 (alpha, 35 kD), eukaryotic translation initiation factor 2A 1733 1324 NM_019371 w EGL nine (C. elegans) homolog 1, EGL nine (C. elegans) homolog 2, EGL nine (C. elegans) homolog 3, EGL nine homolog 3 (C. elegans), ESTs, Moderately similar to A53770 growth factor-responsive protein, vascular smooth muscle - rat [R. norvegicus], ESTs, Weakly similar to A53770 growth factor-responsive protein, vascular smooth muscle - rat [R. norvegicus], SCAN domain- containing 2 1734 19577 NM_019377 e tyrosine 3- monooxgenase/tryptophan 5-monooxgenase activation protein, beta polypeptide, tyrosine 3- monooxygenase/tryptophan 5-monooxygenase activation protein, beta polypeptide 1735 24626 NM_019381 s testis enhanced gene CGI-119 protein, RIKEN cDNA transcript, testis enhanced 5031406P05 gene, testis enhanced gene transcript (BAX gene transcript (BAX inhibitor 1) inhibitor 1) 1736 744 NM_019622 p ESTs, Highly similar to T42716 ankyrin 3, splice form 4 - mouse [M. musculus], ESTs, Moderately similar to A55575 ankyrin 3, long splice form [H. sapiens], ESTs, Weakly similar to T42716 ankyrin 3, splice form 4 - mouse [M. musculus], RIKEN cDNA 2310026G15 gene, RIKEN cDNA 4833425P12 gene, RIKEN cDNA 4930400E23 gene, RIKEN cDNA C430011H06 gene, ankyrin 3, node of Ranvier (ankyrin G), hypothetical protein FLJ20189, phospholipase A2, group VI, phospholipase A2, group VI (cytosolic, calcium-independent), proteasome (prosome, macropain) 26S subunit, non-ATPase, 10 1737 20716 NM_019623 c EST, Weakly similar to CPF1 RAT CYTOCHROME P450 4F1 [R. norvegicus], ESTs, Weakly similar to S45702 leukotriene-B4 20- monooxygenase [H. sapiens], Mus musculus, Similar to RIKEN cDNA 1810054N16 gene, clone MGC: 7384 IMAGE: 3487830, mRNA, complete cds, RIKEN cDNA 2310021J05 gene, cytochrome P450 isoform 4F12, cytochrome P450, subfamily IV B, polypeptide 1, cytochrome P450, subfamily IVF, polypeptide 11, cytochrome P450, subfamily IVF, polypeptide 2, cytochrome P450, subfamily IVF, polypeptide 8, expressed sequence AI787289 1738 20709 NM_019904 x lectin, galactose binding, EST, Moderately similar to 1713410A soluble 1, lectin, beta galactoside soluble lectin galactoside-binding, [H. sapiens], EST, Moderately similar to soluble, 1 (galectin 1) GALECTIN-1 [R. norvegicus], Human HL14 gene encoding beta-galactoside- binding lectin, 3' end, clone 2, RIKEN cDNA 2200008F12 gene, Rattus norvegicus mRNA for galectin-2 related protein, complete cds, lectin, galactose binding, soluble 1, lectin, galactoside-binding, soluble, 1 (galectin 1), lectin, galactoside-binding, soluble, 2 (galectin 2) 1739 574 NM_019905 u, General hydroxyacid oxidase ESTs, Highly similar to (S)-2-(glycolate oxidase) 3, HYDROXY-ACID OXIDASE, hydroxyacid oxidase 3 PEROXISOMAL [R. norvegicus], ESTs, (medium-chain) Highly similar to LUHU36 annexin II [H. sapiens], RIKEN cDNA 1110003P15 gene, RIKEN cDNA B430311C09 gene, annexin A2, annexin A2 pseudogene 2, caspase recruitment domain family, member 6, expressed sequence AW215814, hydroxyacid oxidase (glycolate oxidase) 3, hydroxyacid oxidase 1, liver, hydroxyacid oxidase 2 (long chain), nucleolar protein 3 (apoptosis repressor with CARD domain) 1740 9096 NM_019908 j hypothetical protein similar to mouse aldehyde reductase 6 (renal), renal-specific oxido-reducatse 1741 20457 NM_020073 i, General parathyroid hormone receptor, parathyroid hormone receptor 1 1741 20458 NM_020073 General parathyroid hormone receptor, parathyroid hormone receptor 1 1741 20460 NM_020073 General parathyroid hormone receptor, parathyroid hormone receptor 1 1742 18713 NM_020075 r eukaryotic translation DNA segment, Chr 12, ERATO Doi initiation factor 5 549, expressed, KIAA1856 protein, eukaryotic translation initiation factor 5 1742 18715 NM_020075 r eukaryotic translation DNA segment, Chr 12, ERATO Doi initiation factor 5 549, expressed, KIAA1856

protein, eukaryotic translation initiation factor 5 1743 20493 NM_020076 p 3-hydroxyanthranilate 3,4- dioxygenase, RIKEN cDNA 0610007K21 gene, RIKEN cDNA 0610012J07 gene 1744 16375 NM_020976 g angiotensin I converting enzyme (peptidyl-dipeptidase A) 2, kidney- specific membrane protein 1745 20816 NM_021261 k, General EST, Highly similar to THYMOSIN BETA-10 [R. norvegicus], ESTs, Highly similar to TYB4 MOUSE THYMOSIN BETA-4 [M. musculus], expressed sequence AW544206, thymosin, beta 10, thymosin, beta 4, X chromosome 1746 15335 NM_021264 a ribosomal protein L35a EST, Weakly similar to 60S RIBOSOMAL PROTEIN L35A [R. norvegicus], EST, Weakly similar to R35A MOUSE 60S RIBOSOMAL PROTEIN L35A [M. musculus], EST, Weakly similar to R5HU35 ribosomal protein L35a [H. sapiens], Homo sapiens cDNA FLJ11509 fis, clone HEMBA1002166, RIKEN cDNA 2810431L15 gene, ribosomal protein L35a, uncharacterized hypothalamus protein HSMNP1 1747 18729 NM_021578 k, z transforming growth factor, transforming growth factor, beta 1 beta 1 1748 19060 NM_021587 cc latent transforming growth EST, Weakly similar to TGFB_HUMAN factor beta binding protein 1 LATENT TRANSFORMING GROWTH FACTOR BETA BINDING PROTEIN 1 PRECURSOR [H. sapiens], ESTs, Weakly similar to TGFB RAT LATENT TRANSFORMING GROWTH FACTOR BETA BINDING PROTEIN 1 PRECURSOR [R. norvegicus], RIKEN cDNA 2310046A13 gene, hypothetical protein MGC13010, latent transforming growth factor beta binding protein 1, latent transforming growth factor beta binding protein 2, latent transforming growth factor beta binding protein 3 1749 17324 NM_021593 o, General 1750 19679 NM_021653 General deiodinase, iodothyronine, ESTs, Moderately similar to TYPE I type I IODOTHYRONINE DEIODINASE [R. norvegicus], deiodinase, iodothyronine, type I 1750 19678 NM_021653 a, v, General deiodinase, iodothyronine, ESTs, Moderately similar to TYPE I type I IODOTHYRONINE DEIODINASE [R. norvegicus], deiodinase, iodothyronine, type I

Detail Description Table CWU - DETL (123):

transcription element binding protein 1, trans-acting transcription factor 3, trans-acting transcription factor 6 1888 15052 NM_031136 a ESTs, Highly similar to A38682 thymosin beta-4 [H. sapiens], ESTs, Highly similar to TYB4 MOUSE THYMOSIN BETA-4 [M. musculus], ESTs, Highly similar to TYB4_HUMAN THYMOSIN BETA-4 [H. sapiens], Human interferon-inducible mRNA (cDNA 6-26), expressed sequence AW544206, thymosin, beta 10, thymosin, beta 4, X chromosome, thymosin, beta 4, Y chromosome 1888 19359 NM_031136 a 1889 15185 NM_031140 General EST, Moderately similar to A25074 vimentin [H. sapiens], EST, Weakly similar to A25074 vimentin [H. sapiens], ESTs, Moderately similar to VIME RAT VIMENTIN [R. norvegicus], ESTs, Weakly similar to A25074 vimentin [H. sapiens], ESTs, Weakly similar to VIME RAT VIMENTIN [R. norvegicus], vimentin 1890 21625 NM_031144 a, e EST, Weakly similar to ACTB_HUMAN ACTIN, CYTOPLASMIC 1 [R. norvegicus], ESTs, Highly similar to ATHUB actin beta [H. sapiens], ESTs, Weakly similar to ACTB_HUMAN ACTIN, CYTOPLASMIC 1 [R. norvegicus], Homo sapiens FKSG30 (FKSG30) mRNA, complete cds, RIKEN cDNA 1700052K15 gene, RIKEN cDNA 1700061J02 gene, actin, beta, actin-like 7a, actin-related protein 3-beta, melanoma X-actin 1891 238 NM_031152 bb CATX-8 protein, ESTs, Weakly similar to R11A_HUMAN RAS-RELATED PROTEIN RAB-11A [R. norvegicus], RAB, member of RAS oncogene family like 2A, RAB11A, member RAS oncogene family, RAB11a, member RAS oncogene family, RAB25, member RAS oncogene family, RIKEN cDNA 2700023P08 gene 1891 240 NM_031152 bb CATX-8 protein, ESTs, Weakly similar to R11A_HUMAN RAS-RELATED PROTEIN RAB-11A [R. norvegicus], RAB, member of RAS oncogene family like 2A, RAB11A, member RAS oncogene family, RAB11a, member RAS oncogene family, RAB25, member RAS oncogene family, RIKEN cDNA 2700023P08 gene 1892 15277 NM_031237 g EST, Moderately similar to UB5B_HUMAN UBIQUITIN- CONJUGATING ENZYME E2-17 KD 2 [R. norvegicus], ESTs, Moderately similar to I59365 ubiquitin conjugating enzyme [H. sapiens], ESTs, Moderately similar to UB5B_HUMAN UBIQUITIN- CONJUGATING ENZYME E2-17 KD 2 [M. musculus], RIKEN cDNA 1100001F19 gene, RIKEN cDNA 1600028I17 gene, RIKEN cDNA 2700084L22 gene,

Rattus norvegicus clone ubc2e ubiquitin conjugating enzyme (E217kB) mRNA, complete cds, expressed sequence AL022654, ubiquitin-conjugating enzyme E2D 1 (homologous to yeast UBC4/5), ubiquitin-conjugating enzyme E2D 2, ubiquitin-conjugating enzyme E2D 2 (homologous to yeast UBC4/5), ubiquitin-conjugating enzyme E2D 3 (homologous to yeast UBC4/5) 1893 18083 NM_031315 q ESTs, Weakly similar to YZ28_HUMAN HYPOTHETICAL PROTEIN ZAP128 [H. sapiens], Mus musculus, Similar to cytosolic acyl- CoA thioesterase 1, clone MGC: 27572 IMAGE: 4485973, mRNA, complete cds 1893 1858 NM_031315 q cytosolic acyl-CoA PTE2_HUMAN PEROXISOMAL ACYL- thioesterase 1, COENZYME A THIOESTER peroxisomal long-chain HYDROLASE 2 (PEROXISOMAL acyl-coA thioesterase LONG-CHAIN ACYL-COA THIOESTERASE 2) (ZAP128) [H. sapiens], ESTs, Moderately similar to JE0267 long-chain fatty-acyl-CoA hydrolase (EC 3.1.2 -) peroxisome proliferator-inducible - rat [R. norvegicus], ESTs, Moderately similar to PTE2_HUMAN PEROXISOMAL ACYL-COENZYME A THIOESTER HYDROLASE 2 (PEROXISOMAL LONG-CHAIN ACYL- COA THIOESTERASE 2) (ZAP128) [H. sapiens], ESTs, Weakly similar to PTE2_HUMAN PEROXISOMAL ACYL- COENZYME A THIOESTER HYDROLASE 2 (PEROXISOMAL LONG-CHAIN ACYL-COA THIOESTERASE 2) (ZAP128) [H. sapiens], ESTs, Weakly similar to YZ28_HUMAN HYPOTHETICAL PROTEIN ZAP128 [H. sapiens], Mus musculus, Similar to cytosolic acyl- CoA thioesterase 1, clone MGC: 27572 IMAGE. 4485973, mRNA, complete cds, RIKEN cDNA 4632408A20 gene, cytosolic acyl-CoA thioesterase 1, expressed sequence AW108394, peroxisomal long-chain acyl-coA 1894 15663 NM_031318 General t-complex testis expressed 1, t- complex-associated-testis-ex- pressed 1 like 1 1895 1422 NM_031324 bb, General ESTs, Moderately similar to I38134 prolyl oligopeptidase [H. sapiens], prolyl endopeptidase 1896 18597 NM_031325 g, bb UDP-glucose dehydrogenase 1897 11259 NM_031327 i, cc, General ESTs, Moderately similar to CYR6 MOUSE CYR61 PROTEIN PRECURSOR [M. musculus], cysteine rich protein 61, cysteine-rich, angiogenic inducer, 61 1898 4235 NM_031330 General heterogeneous nuclear ESTs, Highly similar to WZHURS ribonucleoprotein A/B argininosuccinate lyase [H. sapiens], ESTs, Weakly similar to 1601424A argininosuccinate lyase [R. norvegicus], Homo sapiens cDNA FLJ14312 fis, clone PLACE3000322, Musashi-1 homolog (Drosophila), RIKEN cDNA 2510006M18 gene, RIKEN cDNA 4933434H11 gene, argininosuccinate lyase, heterogeneous nuclear ribonucleoprotein A/B, heterogeneous nuclear ribonucleoprotein D-like 1899 18375 NM_031331 l, m EST, Weakly similar to PSD4_HUMAN 26S PROTEASOME REGULATORY SUBUNIT S5A [H. sapiens], ESTs, Moderately similar to PSD4_HUMAN 26S PROTEASOME REGULATORY SUBUNIT S5A [H. sapiens], proteasome (prosome, macropain) 26S subunit, non-ATPase, 4 2221 25419 M22922 a 1900 3519 NM_031334 cc cadherin 1, cadherin 1, ESTs, Weakly similar to I49556 type 1, E-cadherin cadherin-11 - mouse [M. musculus], (epithelial) RIKEN cDNA 2610005L07 gene, cadherin 1, type 1, E-cadherin (epithelial), cadherin 6, cadherin 6, type 2, K-cadherin (fetal kidney) 1901 20698 NM_031357 b 1903 634 NM_031509 n EST, Moderately similar to GTC MOUSE GLUTATHIONE S- TRANSFERASE YC [M. musculus], glutathione S-transferase A3, glutathione S-transferase, alpha 3 1903 25525 NM_031509 n 1903 25069 NM_031509 b, n, w 1903 635 NM_031509 z EST, Moderately similar to GTC MOUSE GLUTATHIONE S- TRANSFERASE YC [M. musculus], glutathione S-transferase A3, glutathione S-transferase, alpha 3 1904 848 NM_031517 t met proto-oncogene, met EST, Highly similar to RON_HUMAN proto-oncogene MACROPHAGE-STIMULATING (hepatocyte growth factor PROTEIN RECEPTOR PRECURSOR receptor) [H. sapiens], ESTs, Highly similar to TVHUME hepatocyte growth factor receptor precursor [H. sapiens], Mus musculus D86 mRNA, complete cds, Rattus norvegicus ryk mRNA for tyrosine kinase-related protein, partial cds, macrophage stimulating 1 receptor (c-met-related tyrosine kinase), met proto-oncogene, met proto-oncogene (hepatocyte growth factor receptor) 1905 1872 NM_031523 a RIKEN cDNA 0610007D04 gene, kallikrein 1, renal/pancreas/salivary, kallikrein 5, kallikrein 9, nerve growth factor, alpha, nerve growth factor, gamma 1905 16245 NM_031523 a, d, u EST,

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non-provisional-of-provisional 60260018 20010105 US

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ABSTRACT:

Disclosed herein are nucleic acid sequences that encode novel polypeptides. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivatives, variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

RELATED APPLICATIONS

[0001] This application claims priority from U.S. Ser. No. 60/260,018, filed Jan. 5, 2001; U.S. Ser. No. 60/260,360, filed Jan. 8, 2001; U.S. Ser. No. 60/272,411 filed Feb. 28, 2001; U.S. Ser. No. 60/272,817 filed Mar. 2, 2001; U.S. Ser. No. 60/291,186, filed May 15, 2001; U.S. Ser. No. 60/303,231, filed Jul. 5, 2001; U.S. Ser. No. 60/305,060 filed Jul. 12, 2001; U.S. Ser. No. 60/318,405, filed Sep. 10, 2001; U.S. Ser. No. and 60/318,700 filed Sep. 12, 2001; each of which is incorporated by reference in its entirety.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (330):
[0327] A search of sequence databases reveals that the NOV12 amino acid sequence has 33 of 34 amino acid residues (97%) identical to, and 34 of 34 amino acid residues (100%) similar to, the 45 amino acid residue ptnr:pir-id:JC5274 protein from human thymosin beta (E=1.6e.sup.-12). Public amino acid databases include the GenBank databases, SwissProt, PDB and PIR.

Summary of Invention Paragraph - BSTX (334):
[0331] Thymosin beta4 is a small polypeptide whose exact physiological role is not yet known [1]. It was first isolated as a thymic hormone that induces terminal deoxynucleotidyltransferase. It is found in high quantity in thymus and spleen but is widely distributed in many tissues. It has also been shown to bind to actin monomers and thus to inhibit actin polymerization [2]. *function: exact physiological role is not yet known. thymic hormone that induces terminal deoxynucleotidyltransferase. can bind to actin monomers and thus to inhibit actin polymerization. *function: hematopoietic system regulatory peptide has inhibitory activity on the proliferation of hematopoeitic pluripotent stem cells. subcellular location: cytoplasmic. *tissue specificity: originally found in thymus but it is widely distributed in many tissues. induction: by alpha-interferon, nerve and fibroblast growth factors. *similarity: belongs to the thymosin beta family. Blocks protein family: BL00500 Thymosin beta-4 family proteins.

Summary of Invention Paragraph - BSTX (335):
[0332] PMID: 2325669, UI: 90220652 Thymosin beta 4 is expressed in ROS 17/2.8 osteosarcoma cells in a regulated manner. Atkinson M J, Freeman M W, Kronenberg H M Endocrine Unit, Massachusetts General Hospital, Boston.

Summary of Invention Paragraph - BSTX (336):

[0333] The differential expression of mRNAs between the closely related rat osteosarcoma cell lines ROS 17/2.8 and ROS 25/1 was used to identify genes whose expression is associated with the osteoblast phenotype. Thymosin beta 4 cDNA was cloned from an ROS 17/2.8 complimentary DAN library on the basis of its differential hybridization with radiolabeled cDNA prepared from ROS 17/2.8 and ROS 25/1 cells. Northern blot analysis confirmed that thymosin beta 4, hitherto a putative immunodulatory hormone, was indeed differentially expressed. Steady state mRNA levels were severalfold higher in ROS 17/2.8 cells exhibiting an osteoblast-like phenotype, compared with the less osteoblast-like ROS 25/1. Thymosin beta 4 transcripts were also detected in rat UMR 106 osteosarcoma cells and in intact neonatal and fetal rat calvaria. Sequence analysis of the cDNA indicated that thymosin beta 4 transcripts may arise by processing at a more distal polyadenylation signal. Treatment of ROS 17/2.8 cells with dexamethasone increased, while addition of 1,25-dihydroxyvitamin D3 decreased thymosin beta 4 mRNA. The phenotype-dependent expression in the ROS cells and the response to steroid hormone suggest that thymosin beta 4 expression contributes to the osteoblast phenotype.

Summary of Invention Paragraph - BSTX (338):

[0335] Thymosin-beta(4) (Theta(4)) binds actin monomers stoichiometrically and maintains the bulk of the actin monomer pool in metazoan cells. Theta(4) binding quenches the fluorescence of N-iodoacetyl-N'-(5-sulfo-1--naphthyl)ethylenediamine (AEDANS) conjugated to Cys(374) of actin monomers. The K(d) of the actin-Theta(4) complex depends on the cation and nucleotide bound to actin but is not affected by the AEDANS probe. The different stabilities are determined primarily by the rates of dissociation. At 25 degrees C., the free energy of Theta(4) binding MgATP-actin is primarily enthalpic in origin but entropic for CaATP-actin. Binding is coupled to the dissociation of bound water molecules, which is greater for CaATP-actin than MgATP-actin monomers. Proteolysis of MgATP-actin, but not CaATP-actin, at Gly(46) on subdomain 2 is >12 times faster when Theta(4) is bound. The C terminus of Theta(4) contacts actin near this cleavage site, at His(40). By tritium exchange, Tbeta(4) slows the exchange rate of approximately eight rapidly exchanging amide protons on actin. We conclude that Theta(4) changes the conformation and structural dynamics ("breathing") of actin monomers. The conformational change may reflect the unique ability of Tbeta(4) to sequester actin monomers and inhibit nucleotide exchange.

Summary of Invention Paragraph - BSTX (344):

[0341] The disclosed NOV12 protein of the invention includes the Thymosin-like protein whose sequence is provided in Table 12B. The invention also includes a mutant or variant protein any of whose residues may be changed from the corresponding residue shown in Table 12B while still encoding a protein that maintains its Thymosin-like activities and physiological functions, or a functional fragment thereof. In the mutant or variant protein, up to about 53 percent of the residues may be so changed.

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FULL ESTIMATED COST                                       1.26       1.26

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11 FILES IN THE FILE LIST

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3 FILES IN THE FILE LIST

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